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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/780,532	02/09/2001	Clive Wood	GNN-012CP	8383

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EXAMINER	
QIAN, CELINE X	
ART UNIT	PAPER NUMBER
1636	

DATE MAILED: 06/01/2005

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/780,532	WOOD ET AL.	
	Examiner	Art Unit	
	Celine X. Qian Ph.D.	1636	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *14 March 2005*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *2,3,5-8,39-43 and 45-65* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *2,3,5-8,39-43 and 45-65* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on *05 July 2001* is/are: a)☒ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

Claims 2, 3, 5-8, 39-43, 45-65 are pending in the application.

This Office Action is in response to the Amendment filed on 3/14/05.

Continued Examination Under 37 CFR 1.114

A request for continued examination under 37 CFR 1.114, including the fee set forth in 37 CFR 1.17(e), was filed in this application after final rejection. Since this application is eligible for continued examination under 37 CFR 1.114, and the fee set forth in 37 CFR 1.17(e) has been timely paid, the finality of the previous Office action has been withdrawn pursuant to 37 CFR 1.114. Applicant's submission filed on 3/14/05 has been entered.

Response to Amendment

The objection to claims 2, 3, 5-8, 39-43 and 45-65 has been withdrawn in light of Applicant's amendment.

The rejection of claims 2, 3, 5-8, 39, 41-43, 45-65 under 35 U.S.C. 112 2nd paragraph has been withdrawn in light of Applicant's amendment of the claims.

The rejection of claims 2, 3, 5-8, 39-43, 45-65 under 35 U.S.C.112 1st paragraph is maintained for reasons set forth of the record mailed on 2/13/04 and further discussed below.

Claim 40 is rejected under 35 U.S.C. 112 2nd for reasons set forth below.

Response to Arguments

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 2, 3, 5-8, 39-43 and 45-65 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

In response to this rejection, Applicants argue that amended claims 2 and 53 are now directed to methods of modulating NFκB activity by contacting cells with polypeptide agents comprising the extracellular domain of a TRADEα polypeptide and having the ability to modulate the activity of a TRADEα polypeptide, wherein the extracellular domain may have 95% sequence identity to amino acid 1-168 of SEQ ID NO:2, or may be encoded by a polynucleotide that hybridizes under stringent condition to the complement of nucleotides 1-504 of SEQ ID NO:1. Applicants assert that the instant claims recite a specific structural and functional relationship for the polypeptide agents to be employed in the claimed methods, thus the rejection should be withdrawn. Applicants further argue that more than one species of TRADEα polypeptides falling within the limitation of the claims are described in the specification. Such species include Flag-TRADEα, Flag-TRADE 1-368, Flag TRADE 1-328, Flag-TRADE 1-218, and Flag-TRADE 1-196, which have ability to modulate NFκB activity as shown in Figures 9 and 14A. Applicants conclude that the specification describes a representative species of the polypeptides that have structural and functional relationship, thus the rejection should be withdrawn.

This argument has been fully considered but deemed unpersuasive. The detailed reasons for lack of sufficient written description of the claimed invention. In response to Applicants'

argument with regard to the structural and functional relationship, the examiner does not agree that the specification has disclosed such relationship between the claimed genus and its function. Applicants are reminded that the claimed genus is a polypeptide agent comprises the extracellular domain of a TRADEα having 95% sequence identity with 1-168 of SEQ ID NO:2, which encompasses a large number of polypeptides of various length and property/function as long as they comprising a domain share 95% sequence similarity with 1-168 of SEQ ID NO:2. As discussed in the previous office action, the cytosolic domain which is C-terminal of SEQ ID NO:2 is responsible for stimulation of NFκB activity. The specification fails to describe a polypeptide that comprises 1-168 of SEQ ID NO:2 or 95% similar to SEQ ID NO:2 having NFκB stimulatory function. As such, the specification fails to describe the claimed genus by a representative number of species by their complete structural and other identifying characteristics.

With regard to Applicants' argument that several species of the claimed genus have been described, Applicants are reminded that not only all of them are fragments of SEQ ID NO:2, but also longer than the claimed domain 1-168. Furthermore, according to the disclosure of the specification and Figure 14. the TRADE 198 and TRADE 218 hardly have any stimulatory effect on NFκB. Moreover, the disclosed species is hardly representative of the entire claimed genus which includes a large number of polypeptides of various length and property/function as long as they comprising a domain share 95% sequence similarity with 1-168 of SEQ ID NO:2. As such, for reasons discussed in the previous office action and above, the specification fails to provide sufficient written description to the claimed invention. Therefore, this rejection is maintained.

Claims 2, 3, 5-8, 39-43 and 45-65 rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the enablement requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention.

In response to this rejection, Applicants argue that the specification provides multiple examples of polypeptides containing the extracellular domain of a TRADEα polypeptide that can modulate the activity of NFκB, including Flag-TRADEα, Flag-TRADE 1-368, Flag TRADE 1-328, Flag-TRADE 1-218, and Flag-TRADE 1-196. Applicants argue that all these polypeptides comprises TRADEα extracellular domain and are able to modulate NFκB promoter driven luciferase activity, thus they clearly fall within the limitation of the present claims. Applicants further argue that since all these polypeptides that modulates the NFκB construct comprises the extracellular domain of the TRADEα, thus it is not unpredictable if they can modulate NFκB signaling. Applicants further assert that the specification clearly establishes a nexus between the claimed method and the modulation of NFκB, and the modulation of TRADEα because Applicants successfully modulated NFκB transcription using various TRADEα polypeptides. Applicants further assert that one skill in the art would also understand that the claimed invention would be useful for treating and preventing any disease that would benefit from the modulation of TRADEα activity or NFκB signaling. Applicants further cite Baldwin to demonstrate that diseases associated with NFκB are well known in the art, thus one skilled in the art would know how to prevent and treat such diseases based on the teaching of the specification. Applicants further assert the method is also useful for identifying agents that modulate TRADEα activity or expression (page 19, lines 20-25). Applicants cite MPEP 2164.01 and conclude the claimed

method is enabled even only one use is enabled when multiple uses are disclosed. Applicants thus conclude that the claimed invention is enabled by the instant specification.

Applicants' argument are fully considered but deemed unpersuasive. The detailed reasons of the non-enablement of the claimed method were discussed in the previous office action. With regard to Applicants' argument of multiple example of polypeptide agents, Applicants are reminded that not only all of them are fragments of SEQ ID NO:2, but also longer than the claimed domain 1-168. Furthermore, according to the disclosure of the specification and Figure 14. the TRADE 198 and TRADE 218 hardly have any stimulatory effect on NFκB. Such disclosure is not sufficient to support the broad claim scope of is a polypeptide agent a polypeptide agent comprises 95% sequence similarity to 1-168 of SEQ ID NO:2, which encompasses a large number of polypeptides of various length and property/function as long as they comprising a domain share 95% sequence similarity with 1-168 of SEQ ID NO:2, to extend the predictability of the modulation activity of such polypeptide agents toward NFκB. Contrary to Applicants' assertion, although there is a nexus between the TRADEα consists sequence of SEQ ID NO:2, the specification fails to establish that a polypeptide agent comprises 95% sequence similarity to 1-168 of SEQ ID NO:2 also have such nexus. Furthermore, the specification fails to disclose that a polypeptide agent comprises 95% sequence similarity to 1-168 of SEQ ID NO:2 have modulating effect toward any TRADEα molecule. Moreover, although prior art, represented by Baldwin et al., demonstrate correlation between NFB pathway and specific disease, the specification fails to teach how to prevent and treat such disease using the claimed method. Lastly, with regard to Applicants' argument to using the claimed method to modulate TRADEα expression/activity *in vitro,* Applicants are again reminded that the

specification does not establish such modulatory function of any polypeptide comprises 95% sequence similarity to 1-168 of SEQ ID NO:2 toward the TRADEα molecule expression and activity. Since prior art is silent on the teaching of the TRADE and its modulatory function and the specification does not teach such self-regulatory function of the TRADEα molecule, one skilled in the art would have to engage in undue experimentation to practice the method as claimed. Therefore, this rejection is maintained.

New Grounds of Rejection

Claim Rejections - 35 USC § 112

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claim 40 is rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

The recitation of "wherein said TRADEα-Fc fusion protein is an isotype selected from the group consisting of 1γ, 2γ, 3γ, ε and α" renders the claim indefinite because it is unclear whether the isotype is refer to the TRADEα, Fc or TRADEα-Fc. Clarification is required.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Celine X. Qian Ph.D. whose telephone number is 571-272-0777. The examiner can normally be reached on 9:30-6:00 M-F.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Remy Yucel Ph.D. can be reached on 571-272-0781. The fax phone number for the organization where this application or proceeding is assigned is 703-872-9306.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

Celine X Qian Ph.D.
Examiner
Art Unit 1636

CELIAN QIAN
PATENT EXAMINER